Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2022-2023

Project Nº 20

Title: *Unleashing tumor immunity by inferring RNA surveillance mechanisms that operate in malignant cells*

Department/ Laboratory *CIMA Department of Molecular Therapy*

Director 1 *Fernando Pastor Rodríguez*
Contact: *fpasrodri@unav.es*

Summary

Tumors evolve acquiring new capabilities allowing them to survive pressing antitumor forces. To achieve this goal tumors display high genomic and transcriptomic plasticity. Evasion of tumor immunity is an important hallmark in cancer progression, but as the tumor acquires new genomic driver mutations it becomes more antigenic being therefore easily recognized by the immune system. We hypothesize that the tumor takes advantage of RNA transcription rewiring and RNA surveillance mechanisms that operate in the cells to preclude the expression of neoantigens derived from de novo acquired mutations. Using bioinformatics analysis of the tumor mutation landscape and transcriptomics, we will interrogate the existence of RNA surveillance forces that impedes the expression of neoantigens. The outcome of this RNA-immunoediting mechanism will be evaluated in different murine tumor models treated with standard immune-checkpoint blockade therapies (with anti-PD(L)-1 and anti-CTLA-4 blocking antibodies). The modulation of immune responses by the RNA surveillance process will be determined by using different in vitro and in vivo immuno assays. The final goal in the long term is the development of a therapeutic agent that counteracts this tumor immunoescape mechanism.

The master's thesis student will be exposed to the following technologies during the timeframe of the master's program: molecular biology techniques (cloning, RNAi, CRISPR and aptamer technology), cell and tissue culture, in vivo animal experiments, different immunoassay techniques, flow cytometry, image confocal microcopy, and different bioinformatic pipelines for omics analysis including scRNAseq.

yes	X
no	

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?